Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Initially, applicants would like to note that the present amendment is being submitted in compliance with "Amendments In A Revised Format Now Permitted", 1267 OG 4 (February 25, 2003). Pursuant to this notice, the requirements of 37 C.F.R. § 1.121 have been waived.

Applicants wish to thank the Examiner for the courtesy extended to applicants' undersigned representative during the telephone conference on November 8, 2002. The substance of the telephone conference is reflected below.

Enclosed herewith is a Declaration of Michael Krogh Under 37 CFR § 1.132 ("Krogh Decl."). Mr Krogh states that he is a quality manager of Gentra Systems (Krogh Decl. ¶ 1), the company which produces HYB-9® Hybridization Solution (Id. ¶ 2). Mr. Krogh confirms that the sodium content of the HYB-9® Hybridization Solution is about 1.7M (Id. ¶ 3). This disclosure is being relied upon for purposes of amending the claim language of claim 1 to recite the sodium content of the hybridization medium being employed. Example 5 recites that HYB-9® Hybridization Solution was used in the DNA gel blot procedure described therein. Thus, descriptive support exists for this amendment and no new matter has been added.

While applicants do not admit that the combined declaration and power of attorney as submitted is defective, enclosed herewith is a newly executed combined declaration and power of attorney. Therefore, this objection should be withdrawn.

The objections to the specification have been overcome by the amendments to the description of the drawings so as to include sequence identification numbers therein. Therefore, this objection should be withdrawn. A revised sequence listing in paper form and computer readable form are also enclosed, along with statements under 37 C.F.R. § 1.821(f)-(g). Applicants request entry of the revised sequence listing into the application.

The rejection of claims 1-10 under 35 U.S.C. § 112 (first paragraph) for want of written descriptive support for the phrase "a DNA molecule from a source other than *Pseudomonas syringae* pv. *tomato*", appearing in claim 1, is respectfully traversed.

During the November 8, 2002, telephone conference, the U.S. Patent & Trademark Office ("PTO") asserted that the above-quoted language must appear in the specification for adequate written descriptive support to exist. Applicants respectfully disagree.

It is well established law that satisfaction of the written description requirement does not require *ipsis verbis* support in the specification. See In re Wertheim, 541 F.2d 257, 265, 191 USPQ 90, 98 (CCPA 1976) (citing In re Lukach, 442 F.2d 967, 969, 169 USPQ 795, 796 (CCPA 1971)). Instead, the specification need only demonstrate to one of ordinary skill in the art that applicants invented the claimed subject matter. See In re Gostelli, 872 F.2d 1008, 1012 (Fed. Cir. 1989); Union Oil Co. v. Atlantic Richfield Co., 208 F.3d 989, 1001, 54 USPQ2d 1227, 1232 (Fed. Cir. 2000).

Claim 1 relates to an isolated DNA molecule that comprises, *inter alia*, "(c) a DNA molecule from a source other than *Pseudomonas syringae* pv. *tomato* which hybridizes to a DNA molecule comprising the complement of SEQ ID NO: 1 under hybridization conditions comprising hybridization at 62°C for 8 hours in a hybridization medium that contains about 1.7M Na^+ followed by wash conditions effective to remove DNA that binds non-specifically to the DNA molecule comprising the complement of SEQ ID NO: 1...." Applicants submit that sufficient written descriptive support exists for the above-noted language, specifically at Examples 5 and 10 of the specification (at pages 24-25 and 28-29, respectively). Example 5 defines the above-identified hybridization conditions and exemplary wash conditions for the hybridization procedure employed, a DNA gel blot using enzyme-digested DNA from eleven representative Gram-negative plant pathogens. The actual blot results are illustrated in Figure 3. Under the recited conditions, the full-length *hrpW* probe hybridized to isolated DNA molecules from not only *Pseudomonas syringae* pv. *tomato* (as control) but also isolated DNA molecules from sources other than *Pseudomonas syringae* pv. *tomato*, including *Pseudomonas syringae* pv. *glycinea*, *Pseudomonas syringae* pv. *papulans*, *Pseudomonas syringae* pv. *pisi*, *Pseudomonas syringae* pv. *phaseolicola*, *Pseudomonas syringae* pv. *tabaci*, *Pseudomonas syringae* pv. *syringae* strains B728a and 61, *Pseudomonas viridiflava*, *Ralstonia solanacearum*, and *Xanthomonas campestris* pv. *amoraciae*, and *Xanthomonas campestris* pv. *vesicatoria*. Thus, applicants have clearly identified that they were in possession of isolated DNA molecules from sources other than *Pseudomonas syringae* pv. *tomato* that hybridize to the DNA of SEQ ID NO: 1.

Furthermore, the above-noted language was introduced for purposes of explicitly excluding from the subject matter of subparagraph (c), quoted above, the nucleic acid identified by Lorang et al., Mol. Plant-Microbe Interact., 8:49-57 (1995) ("Lorang").

Specifically, in Figure 3 of Lorang, a nucleotide sequence from *Pseudomonas syringae* pv. *tomato* DC3000 is shown which contains two distinct transcriptional units, IV and V. With the partial sequence of transcriptional unit V, Lorang at Figure 3 discloses a portion of the nucleotide sequence of SEQ ID NO: 1. Lorang is expressly incorporated by reference into the specification of the present application (see page 5, line 14; page 27, lines 8 and 23; page 31, line 12; and page 33, line 19). Thus, the subject matter of Lorang is contained in the present application and such subject matter is excluded from the scope of claim 1 by the objected limitation. Because the present application provides sufficient written descriptive support for the genus as originally claimed and the present application provides sufficient written descriptive support for the subject matter being excluded (by the objected limitation), applicants submit that sufficient written descriptive support also exists for the subgenus presently claimed.

For all these reasons, the above-identified phrase is not new matter and the rejection of claims 1-10 for lack of written descriptive support should be withdrawn.

The rejection of claims 1 and 4-10 under 35 U.S.C. § 112 (first paragraph) for lack of enablement is respectfully traversed in view of the above amendments and the following remarks.

Initially, applicants note that the comments concerning plant transformation was rendered moot by the cancellation of those claims without prejudice in the amendment filed March 18, 2002. Because claims directed to that subject matter have been withdrawn, applicants need not respond to the objections made by the PTO.

The basis of the rejection of claims 1 and 4-10 is that the specification "does not reasonably provide enablement for nucleic acids that hybridize under conditions of unspecified stringency to SEQ ID NO: 1" (office action at page 3). Applicants submit that the above amendments overcome the basis of the rejection because the hybridization conditions have been specified in sufficient detail to enable one of ordinary skill in the art to determine whether a given DNA molecule hybridizes to the complement of SEQ ID NO: 1 and whether the DNA molecule encodes a hypersensitive response elicitor.

With respect to the stringency of hybridization, the above amendments specify the time, temperature, and sodium concentration for the hybridization conditions and that the wash conditions are those which are "effective to remove DNA that binds non-specifically to the DNA molecule comprising the complement of SEQ ID NO: 1." Applicants submit that one of ordinary skill in the art is fully enabled to practice the presently claimed invention.

Given the recitation of the hybridization conditions, one of ordinary skill in the art would have been able to carry out the hybridization in August 1997. The only issue, therefore, is whether one of ordinary skill in the art would have been enabled to perform the subsequent wash steps. It is well established law that matter which is known to those of ordinary skill in the art need not be included in the specification. See Paperless Accounting, Inc. v. Bay Area Rapid Transit Sys., 804 F.2d 659, 664, 231 USPQ 649, 653 (Fed. Cir. 1986) ("A patent applicant need not include in the specification that which is already known to and available to the public."). In fact, a patent preferably omits that which is well known in the art. Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).

In considering the enablement of the presently claimed invention, therefore, it is appropriate to consider what was known in the art in August 1997 (when applicants filed their priority application). At that time, it was well known to those of ordinary skill in the art that hybrids formed between DNA molecules of more than 200 nucleotides in length are completely stable for all practical purposes (see Sambrook et al., Molecular Cloning: A Laboratory Manual, 2d ed., Cold Spring Harbor Laboratory (1989) at 11.45 ("Sambrook") (copy attached as Exhibit A)). As a result, hybrids formed when using DNA molecules of more than 200 nucleotides are essentially stable under the conditions used for post-hybridization washing (Id.). In contrast, shorter nucleotides are not so stable and, therefore, they can be removed easily during post-hybridization washing (Id.). According to Sambrook et al., post-hybridization washing should be carried out briefly under low stringency conditions and then under conditions of stringency comparable to those used for hybridization (Id.).

SEQ ID NO: 1 and its complement are larger than 200 nucleotides in length. Thus, one of ordinary skill in the art would understand that post-hybridization wash conditions could be performed as described by Sambrook. Given the state of the art in hybridization techniques in August 1997, one of ordinary skill in the art would be fully capable of performing wash procedures, even several wash procedures of increasing stringency, without undue experimentation. Given that one of ordinary skill in the art would have been fully able to practice the presently claimed invention to identify DNA molecules that hybridize to SEQ ID NO: 1 (or its complement), the rejection of claims 1 and 4-10 on the basis of the hybridization specificity is improper and should be withdrawn.

Moreover, given applicants identification of a single species of *hrpW* by its nucleotide sequence (as well as the amino acid sequence of its encoded HrpW protein) and the demonstration that HrpW homologs exist in other Gram-negative pathogens (e.g.,

Pseudomonas syringae pathovars *glycinea*, *papulans*, *pisi*, *phaseolicola*, *tabaci*, and *syringae* strains B728a and 61, *Pseudomonas viridiflava*, *Ralstonia solanacearum*, and *Xanthomonas campestris* pathovars *amoraciae* and *vesicatoria*), one of ordinary skill in the art would have expected HrpW to be distributed widely among Gram negative pathogens. This fact is further evidenced by the post-filing date demonstration, by routine Southern hybridization, that HrpW is indeed widely dispersed among Gram negative pathogens (see Guttman et al., "A Functional Screen for the Type III (Hrp) Secretome of the Plant Pathogen *Pseudomonas syringae*," Science 295:1722-1726 (2002) ("Guttman") at Table 3)(reporting distribution of HrpW among *Pseudomonas syringae* pathovars *maculicola*, *phaseolicola*, *tomato*, and *syringae*, as well as *Pseudomonas* species *viridflava*, *chicorii*, *fluorescence*, *putida*, *stutzeri*, *aeruginosa*, and *Ralstonia solanacearum*, *Xanthomonas campestris* pv. *campestris*, and *Burkholderia capacia*) (copy attached as Exhibit B). The Southern procedure described by Guttman relies on the Southern protocol of Sambrook (see Guttman, Table 3 description and citation to reference '45'). The later work of Guttman therefore supports applicants' claim to the isolated DNA molecule of claim 1.

Applicants further submit that one of ordinary skill would have been fully able to express the protein from a DNA molecule hybridizing to the complement of SEQ ID NO: 1 (see specification at page 11, line 7 to page 14, line 23, describing recombinant techniques and protein purification procedures) and then determine whether the encoded protein does in fact elicit a hypersensitive response when infiltrated onto non-host plants. As demonstrated in Example 11 of the present application, the protein preparation can be infiltrated onto tobacco leaves to assay whether a hypersensitive response-like necrosis is induced (see specification at page 29, lines 22 and Figure 5).

In addition, the HrpW protein of SEQ ID NO: 2 is disclosed in the present application to share properties with other known hypersensitive response elicitors, including: amino acid composition, heat-stability, low mobility in SDS-PAGE, and ability to elicit a hypersensitive response (see specification at page 31, lines 19-24). That these properties are shared by the art-recognized class of proteinaceous hypersensitive response elicitors is evident not only in the specification, but also in the prior art (see Bonas I, Bonas II, Preston, cited in and attached to response submitted on March 18, 2002). (The fact that applicants did not cite Bonas I, Bonas II, and Preston in the specification is irrelevant to the issue of enablement because, for the reasons noted above, one of ordinary skill in the art is presumed to possess such knowledge in the prior art.) Thus, one of ordinary skill in the art would also have been able to assess whether the protein or polypeptide encoded by a hybridizing DNA

molecule shares these properties with other members of the art-recognized class of hypersensitive response elicitor proteins.

For all these reasons, the rejection of claims 1 and 4-10 for lack of enablement is improper and should be withdrawn.

The rejection of claims 1 and 4-10 under 35 U.S.C. § 112 (first paragraph) for lack of written descriptive support is respectfully traversed. The basis of this rejection is that the hybridization conditions are not recited with specificity and the activity of the protein is not recited. Applicants respectfully disagree.

For substantially the same reasons as noted above, one of ordinary skill in the art would fully recognize that applicants were in possession of isolated DNA molecules from sources other than *Pseudomonas syringae* pv. *tomato* that encode HrpW homologs. Applicants have demonstrated that *hrpW* is indeed widespread among Gram negative pathogens and, like other hypersensitive response elicitors, HrpW is characterized by an ability to elicit a hypersensitive response-like necrosis in non-host plant tissues. Therefore, written descriptive support does indeed exist for the presently claimed invention given the above amendments to specify hybridization conditions.

As for the activity of the encoded protein, Claim 1 recites that the DNA molecule encodes a "hypersensitive response eliciting protein or polypeptide...." This activity of the protein is described at page 31, lines 19-24.

For these reasons, the rejection of claims 1 and 4-10 for lack of written descriptive support is improper and should be withdrawn.

The rejection of claims 1-10 under 35 U.S.C. § 112 (second paragraph) for indefiniteness is respectfully traversed in view of the above amendments specifying the limitations of the hybridization conditions and the wash conditions. Therefore, this rejection should be withdrawn.

The rejection of claims 1 and 4-10 under 35 U.S.C. § 102(a) as being anticipated by Tabakaki et al., "Expression of the *Pseudomonas syringae* pv. *phaseolicola hrpZ* Gene in Transgenic Tobacco and *Saccharomyces cerevisiae*," In Developments in Plant Pathology: Pseudomonas Syringae Pathovars and Related Pathogens, Rudolph et al. (eds.), Kluwer Acad. Publ. (Norwell, MA) pp. 392-396 (1997) ("Tabakaki") is respectfully traversed. The PTO cites Tabakaki for the proposition that the *hrpZ* gene would share at least one nucleotide with SEQ ID NO: 1 and its encoded protein would share at least one amino acid with the protein of SEQ ID NO: 2. Applicants submit that the PTO's position is

obviated by the above amendments, because Tabakaki does not teach a DNA molecule as recited in claim 1. (The PTO conceded in the November 8 telephone conference that amendments sufficient to overcome the above-noted rejections under section 112 will necessarily overcome the rejection based on Tabakaki.) Therefore, the rejection of claims 1 and 4-10 should be withdrawn.

The rejection of claims 1 and 4-10 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,850,015 to Bauer et al. ("Bauer '015 patent") is respectfully traversed. The PTO cites to the Bauer '015 patent for the proposition that the *hrpN*$_{Ech}$ gene would share at least one nucleotide with SEQ ID NO: 1 and its encoded protein would share at least one amino acid with the protein of SEQ ID NO: 2. Applicants submit that the PTO's position is obviated by the above amendments, because the Bauer '015 patent does not teach a DNA molecule as recited in claim 1. (The PTO conceded in the November 8 telephone conference that amendments sufficient to overcome the above-noted rejections under section 112 will necessarily overcome the rejection based on the Bauer '015 patent.) Therefore, the rejection of claims 1 and 4-10 should be withdrawn.

In view of all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

Date: April 15, 2003

Edwin V. Merkel
Registration No. 40,087

NIXON PEABODY LLP
Clinton Square, P.O. Box 31051
Rochester, New York 14603-1051
Telephone: (585) 263-1128
Facsimile: (585) 263-1600

Certificate of Mailing - 37 CFR 1.8(a)
I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: U.S. Patent and Trademark Office P.O. BOX 2327 Arlington, VA 22202, on the date below.
Date 4/15/03 Jane C. Wirszyla